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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KOLKER, DANIEL E	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 08/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/791,166	CHARO ET AL.	
	Examiner	Art Unit	
	Daniel Kolker	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,7,10 and 13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,7,10,13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The remarks and amendments filed 22 May 2006 have been entered. Claims 2 – 3, 5 – 6, 8 – 9, 11 – 12, and 14 – 18 are canceled; claims 1, 4, 7, 10, and 13 are pending.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Continued Examination Under 37 CFR 1.114

3. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 22 May 2006 has been entered.

Withdrawn Rejections and Objections

4. The following objections and rejections made in the previous office action are withdrawn in light of applicant's amendments.

A) All rejections of claims now canceled are moot.

Maintained Rejections and Objections

Priority

5. The effective filing date for all pending claims is 1 March 2004 for the reasons made of record previously. The instant application claims priority to several previously-filed applications, the earliest of which was filed 13 January 1994. The specification of the instant application appears to be identical to some of the previously-filed applications. Applicant argues, beginning on p. 5 of the remarks filed 22 May 2006, that the previously-filed applications all provide adequeate support of the invention now claimed in the manner required by 35 USC 112, first paragraph, and thus applicant is entitled, under 35 USC 120, to an effective filing date of 13 January 1995, the date that application 08/446669 (now US 6,132,987) was filed. Before touching on the merits of applicant's arguments, the examiner notes that 08/446669 was filed 25 May 1995, not 13 January 1995, as applicant asserts on p. 5 of the remarks. No application was filed 13 January 1995, although PCT/US95/00476, which has an identical specification as 08/446669, the latter being a national-stage entry of the former, was filed 11 January 1995.

While it is not entirely clear which date applicant is attempting to claim as the effective filing date of the invention now claimed, the point is moot as neither application discloses the invention now claimed. What is clear is that applicant is no longer arguing that 08/182962, filed 13 January 1994, provides sufficient disclosure of the invention now claimed.

This priority determination is maintained for the reasons of record. Applicant's arguments as to why he is entitled to the earlier priority date are addressed below.

On p. 5 of the remarks filed 22 May 2006, applicant argues that the '987 patent incorporates by reference US Patent 5,194,375, and that the '375 patent "teaches use of monoclonal antibodies as antagonists for receptor proteins" (remarks, p. 5). The '987 patent, as well as the instant application, does in fact incorporate by reference that "binding assays similar to those described for IL-7 is U.S. Pat. No. 5,194,375 may be used." (instant specification, paragraph [0087], and '987 patent column 16, lines 58 – 59). Applicant is reminded of the guidance set forth in MPEP § 608.01(p)(I)(A). Applicant is referred to the quotation of this section which the examiner set forth on p. 5 of the final rejection mailed 18 November 2005. No specific columns of the '375 patent were referred to, although clearly the relevant subject matter, incorporated by reference, is the binding assays. Column 16 line 58 of the '987 patent does not discuss antibodies in general or monoclonals in particular. It clearly refers to the binding assays of the '375 patent. These binding assays are described in 5,194,375 at column 14, line 5 – column 15 line 26. Applicant argues, at the top of p. 6 of the remarks that since the '375 patent also discloses antibodies to IL-7, the incorporation-by-reference is sufficient to incorporate all the teachings of the patent, and that applicant clearly contemplated use of monoclonal antibodies to the MCP-1 receptor for treatment of disease at the time the application for the '987 patent was filed.

Applicant's arguments have been fully considered but they are not persuasive. The instant specification does not disclose treatment of diseases characterized by monocytic infiltration by administering monoclonal antibodies to the MCP-1 receptor. There is no disclosure of this method in the instant specification or in any of the previously-filed applications. The fact that the '375 patent teaches how to make monoclonal antibodies is of no relevance, because that subject matter was not referred to in the instant specification or in any of the previously-filed applications. The only part of the '375 patent that was referred to, and therefore the only section that was properly incorporated by reference, was the section on binding assays.

Applicant also argues that the methods set forth in US Patent 4,411,993 could be adapted to make anti MCP-1 monoclonal antibodies, and that since this is true the pending claims are entitled to the benefit of the date that 08/446669 was filed. Applicant's arguments have been fully considered but they are not persuasive. First, the examiner is unable to find any incorporation by reference of US Patent 4,411,993 in the text of the instant specification or in the '987 patent. The '993 patent was not incorporated by reference into either. If the method of making monoclonal antibodies from 4,411,993 had been incorporated by reference, applicant's arguments might in fact be persuasive. However, there appears to be no conception of methods of making monoclonal antibodies in the '987 patent (a text search of the specification revealed zero hits for "monoclonal" or "hybridoma"), thus whether or not the methods of making monoclonals were known in the prior art is not relevant.

None of the previously-filed specifications disclose the methods now claimed, which include administration of antibodies in general, and monoclonals in particular, to patients for treatment of diseases. While administration of antagonists generally is discussed in the instant specification at paragraph [0018] and at column 6 lines 12 – 16 of the '987 patent, neither one defines "antagonist" to include antibodies in general or monoclonal antibodies in particular. Applicant did not disclose these methods until submission of the original claims of the instant application on 1 March 2004 (see original claims 1 – 3, 5, and 7, for example). Therefore, the effective filing date remains 1 March 2004.

Claim Rejections - 35 USC § 112

6. Claims 1, 4, 7, 10, and 13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for administration of anti-MCP-1 receptor antibodies, does not reasonably provide enablement for determination of "a therapeutically effective amount" of the antibody. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This rejection is maintained for the reasons made of record in the previous office action.

The scope of claim 1 now is limited to rheumatoid arthritis, alveolitis, and atherosclerosis. Applicant argues that these three conditions were known to be mediated by MCP-1. Applicant's arguments are persuasive on this point, so the amendments and

arguments are sufficient to overcome the rejection to the extent that it was made for unreasonable breadth related to conditions to be treated.

However, the specification does not provide sufficient guidance for the skilled artisan to determine what constitutes a therapeutically effective amount of the antibodies. Applicant argues, on p. 9 of the remarks that the specification in fact provides guidance as to what constitutes a therapeutically effective amount of the antibody at paragraph [0084]. However that paragraph is on point to the amount of an organic compound to be used in a screening assay to identify MCP-1 antagonists. It does not indicate if the amount used in the screening assay is therapeutically effective, which is recited in both independent claims 1 and 10. Applicant agues that paragraphs [0130] and [0135] teach how measure chemotaxis and calcium, and that these teachings are sufficient to allow the artisan to determine how much antibody is effective in treatment of patients. These paragraphs discuss how MCP-1 activation was measured, but do not teach the artisan how much antibody should be administered to patients in order to treat conditions, as recited in claim 1, or to inhibit MCP-1 activation, as recited in claim 10.

Applicant argues on p. 9 of the remarks, that testing of an antibody is routine. While testing of antibodies is within the skill of the artisan, the specification provides no working examples of any disease or condition actually treated by administration of the antibodies. The specification does not provide any working examples of in vitro inhibition of MCP-1 receptor activation by contacting any cells with antibodies. The only guidance in the specification is that an antagonist of any structure should be used at 10 ug/ml - 1 mg/ml. This of course is a very wide range and covers 2 orders of magnitude. Additionally, it refers only to the concentration of the antagonist in solution, and has nothing to do with the dose that is actually administered to the patient. There is no indication if the amount administered should be on the order of micrograms or milligrams, or even more. Thus given the complete lack of disclosure of the efficacy or potency of the antibodies in treatment of conditions and inhibition of MCP-1 receptor activation, the absence of any working examples of the antibodies being able to accomplish any of these, the broad range of concentrations (not doses) said to be effective, it would take undue experimentation on the part of the skilled artisan to determine what constitutes a therapeutically effective amount of the antibodies to be used in the claimed methods.

7. Claims 1, 4, 7, 10, and 13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

This rejection is maintained for the reasons of record. The specification as originally filed clearly does not disclose monoclonal antibodies, nor does it disclose hybridomas, which make monoclonal antibodies. The specification does not disclose administration of antibodies for treatment of disease, nor does it disclose administration of a composition containing 10 ug/ml – 1 mg/ml antibody, thereby still constituting new matter.

Applicant argues, on p. 10 of the remarks, that the specification teaches the artisan how to identify antagonists at paragraphs 0084 and 0085. While true, identification of antagonists is not what is now claimed, administration of antibodies to patients is what is now claimed. Applicant also argues that what is well-known or conventional need not be explicitly described in the specification, and cites *Hybridtech* and *Noelle*.

Applicant's arguments have been fully considered but they are not persuasive. Applicant is reminded that the claims are drawn to methods for inhibiting conditions (claim 1) and MCP-1 receptor activation (claim 10). While antibodies must be administered, they are not themselves claimed. Thus quotation from *Noelle* is not on point; while the protein sequences are disclosed, the antibodies which bind to them are not what is now claimed. Rather the methods of treatment by administering antibodies are now claimed, and the specification as originally filed simply does not disclose these methods. While applicant is of course correct that what is well-known need not be described in the specification, treatment of conditions and inhibition of MCP-1 receptor activation by administering antibodies which bind to SEQ ID NO:2 or 4 was not well-known at the time the disclosure was filed, nor is it described in the specification. Therefore, the rejection stands for the reasons of record. Applicant is referred to the section entitled Priority, above, for a more detailed explanation of how the instant specification, as well as those previously-filed, fail to disclose that applicant had in his possession the invention now claimed.

Claim Rejections - 35 USC §§ 102 and 103

8. Claims 1, 7, 10, and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by LaRosa et al. (U.S. Patent 6,312,689, cited by applicant on IDS filed 20 May 2005). This rejection is maintained for the reasons made of record in the previous office action. Applicant

argues that the effective filing date of the instant application is 11 January 1995. However as explained in the section entitled "priority" above, there was *no contemplation* of administration of antibodies prior to the filing of the instant application. Therefore the effective filing date is the date the instant application was filed, specifically 1 March 2004. Applicant did not traverse the examiner's determination that LaRosa teaches the method now claimed, but only traversed the issue of priority and effective filing date. As the effective filing date is 1 March 2004, the rejection stands for the reasons of record.

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed applications fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application, as set forth in detail above in the section entitled "Priority" above.

9. Claims 1, 4, 7, 10, and 13 are rejected under 35 U.S.C. 103(a) as obvious over LaRosa et al. for the reasons made of record in the previous office action. Applicant argues that the effective filing date of the instant application is 11 January 1995. However as explained in the section entitled "priority" above, there was *no contemplation* of administration of antibodies prior to the filing of the instant application. Therefore the effective filing date is the date the instant application was filed, specifically 1 March 2004. Applicant did not traverse the examiner's determination that LaRosa teaches the method now claimed, but only traversed the issue of priority and effective filing date. As the effective filing date is 1 March 2004, the rejection stands for the reasons of record.

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

DK

Daniel E. Kolker, Ph.D.
August 1, 2006

RCH

ROBERT C. HAYES, PH.D.
PRIMARY EXAMINER